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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 07/402,450
Filing Date: September 01, 1989
Appellant(s): MURAKAWA ET AL.

Jeffrey L. Ihnen
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on January 25, 2010 appealing from the Office action mailed December 23, 2008.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 190-225, 242-245 and 249-255 are pending.

Claims 1-189, 226-241 and 246-248 have been canceled.

Claims 190-225, 242-245 and 249-255 have been rejected.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

5,219,727	***WANG et al.***	***6-1993***
4,683,195	***MULLIS et al.***	***7-1987***

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections -35 USC 5 135(b)

1. The following is a quotation of 35 U.S.C. 135(b)(l) which forms the basis for all the rejections set forth in this Office action: (b)(l) A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless such a claim is made prior to one year from the date on which the patent was granted. 5. Claims114,115,117,118,120,122,123,125,126,128,130,131,133,134, 208-210, 212, 213,215, 217-219,221, 222, 224 and 226-248 are rejected under 35 U.S.C. 135(b)(l) as not being made prior to one year from the date on which U.S. Patent No. 5,219,727 was granted. See In re McGrew, 120 F.3d 1236, 1238,43 USPQ2d 1632,1635 (Fed. Cir. 1997) where the Court held that 35 U.S.C. 135(b) may be used as a basis for ex parte rejections. Wang teaches a method of claims 114, 122, 130, 138, 146, 190, 199, 208,217, 226, a process for quantitation of a target viral RNA in a sample which comprises (see claim 1, "method for quantifying a target nucleic acid segment in a sample" and claim 8, where the sequence may be from HIV, which is an RNA virus), (i)

selecting a sequence present in the target viral RNA; (see claim 1,"(a) adding to said sample a predetermined initial amount of standard nucleic acid segment wherein said standard nucleic acid segment binds to same primers as are bound by 'said target nucleic acid segment in a reaction mixture", where a target nucleic acid sequence is selected), (ii) adding a known quantity of a reference RNA sequence to the sample, wherein the reference RNA sequence consists of the selected target viral RNA sequence with a

multibase insert into a site within the selected target viral RNA sequence, wherein the reference RNA sequence and the selected target viral RNA sequence are of similar length and can be amplified and detected by the same oligonucleotides and wherein following amplification amplified reference RNA sequence and amplified selected target viral RNA sequence are distinguishable by size or by probe (see claim 1, "(a) adding to said sample a predetermined initial amount of standard nucleic acid segment wherein said standard nucleic acid segment binds to same primers as are bound by said target nucleic acid segment in a reaction mixture", where a target nucleic acid sequence is selected", and step b of claim 1, "(b) treating said sample under conditions suitable for carrying out a polymerase chain reaction, wherein said nucleic acids are rendered single-stranded and exposed to an agent for polymerization, deoxynucleoside 5' triphosphates, and a pair of oligonucleotide primers, wherein said pair of primers is specific for both the target and standard nucleic acid segments, such that an extension product of each primer of said pair can be synthesized using separate strands of the target and standard segments as a template for synthesis, such that the extension product of one primer, when it is separated from the template strand, can serve as a template for the synthesis of the extension product of the other primer of said pair wherein said amplified target and standard segments are distinguishable by

size or by the use of internal probes, wherein said internal probes may be differentially labeled for each of said amplified target and standard segments; where Wang teaches references and Targets that are amplified by the same oligonucleotides and see claim 6, where the ' target is within an mRNA sequence and see figures 2 and 3, where the size renders the target and reference distinguishable), (iii) simultaneously subjecting the selected target viral RNA sequence and the reference RNA sequence in the sample to polymerase chain reaction amplification under conditions appropriate to simultaneously amplify the selected target viral RNA sequence if present in the sample and the reference RNA sequence (see step (b) of claim 1 of Wang, "(b) treating said sample under conditions suitable for carrying out a polymerase chain reaction, wherein said nucleic acids are rendered single-stranded and exposed to an agent for polymerization, deoxynucleoside 5' triphosphates, and a pair of oligonucleotide primers, wherein said pair of primers is specific for both the target and standard nucleic acid segments, such that an extension product of each primer of said pair can be synthesized using separate strands of the target and standard segments as a template for synthesis, such that the extension product of one primer, when it is separated from the template strand, can serve as a template for the synthesis of the extension product of the other primer of said pair wherein said amplified target and standard segments are distinguishable by size or by the use of internal probes, wherein said internal probes may be differentially labeled for each of said amplified target and standard segments;; (iv) measuring the amounts of the amplified selected target viral RNA sequence and the amplified reference RNA sequence; (see step (e) of claim 1 of Wang, (e) measuring the amounts of the amplified target and standard segments produced in step (dl); (v) determining the amount of the target viral RNA present in the sample before amplification from the amount of the

amplified selected target viral RNA sequence and the amount of the amplified reference RNA sequence (see claim 1, step (f) of Wang, "calculating from the amplified target and standard segments produced in step (d) the amount of said target nucleic acid segment present in the sample before amplification.") With regard to claims 115, 123, 131, 139, 147, 149, 192, 201,210,219,228, Wang teaches the analysis of HIV (see claim 8, where HIV proteins are analyzed). With regard to claim 117, 125, 133, 141, 194,203, 212,221, Wang teaches measurement of the amount of amplified target and reference RNA signals (see claim 6 of Wang, "The method of claim 4 wherein the pair of oligonucleotide primers of step (b) is labeled, and the amounts of amplified target and standard segments produced are measured according to step (e) by determining the amount of label incorporated into each of said amplified nucleic acid segments.") With regard to claims 118, 120, 126, 128, 134, 136, 142, 144, 195, 197,204, 206,213,215,222,224, Wang teaches the use of labeled probes and primers (see claim 6). With regard to claim 148, Wang teaches a reverse transcription reaction (see claim 4) and teaches the other elements as discussed in the base rejection above. With regard to claims 150-151, 229-234, the BPAI in the decision in Paper 36, expressly barred claims 46 and 47, which were drawn to the reaction mixtures identical to claims 150 and 151 by the Wang patent.

With regard to claims 191,200, 209,218, 227, Wang teaches internal sequences which include unrelated sequences (see claim 5, drawn to the AW108 plasmids which have unrelated sequences as shown in figure 1). With regard to claims 235-248, Wang teaches the use of multiple multibase inserts, each of which is about 21 bases in length (see claim 5 and figure 1 and especially claim 10, where the inserts are each approximately 21 base pairs in length).

2. Claims 116, 119, 121, 124, 127, 129, 132, 135, 137, 139, 140, 143, 145, 193, 196, 198,202,205,207,211,214,220,223 and 225 are rejected under 35 U.S.C. 135(b)(l)as not being made prior to one year from the date on which U.S. Patent No. 5,219,727 was granted in view of Mullis et al (U.S. Patent 4,683,195). See in re McGrew, 120 F.3d 1236, 1238,43 USPQ2d 1632, 1635 (Fed. Cir. 1997) where the Court held that 35 U.S.C. 135(b) may be used as a basis for ex parte rejections. Wang teaches the limitations of claims 114, 115, 117, 118, 120, 122, 123, 125, 126, 128, 130, 131, 133, 134, 136, 138, 141, 142, 144, 146-151, 190-192, 194, 195, 197, 199-201,203,204,206,208-210,212,213,215,217-219,221, 222,224 and 226-248 as discussed above. Wang does not teach the use of T7 promoters on primers or radioisotopes. Mullis teaches the use of T7 promoters (see column 29, lines 40-50) as well as the use of radioisotopes (see column 25, line 34). lt would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the T7 promoters and radioisotopes of Mullis in the invention of Wang in order to permit easier detection using the radiolabel and in order to express more RNA when desired as taught by Mullis. As the Federal Circuit has noted in DvStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 80 USPQ2d 1641, 1651 (Fed. Cir. 2006), Indeed, we have repeatedly held that an implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as a whole, but when the "improvement" is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient. Because the desire to enhance commercial opportunities by improving a product or process is universal-and even common-sensical-we have held that there exists in these situations a motivation to combine prior art references even absent

any hint of suggestion in the references themselves. In such situations, the proper question is whether the ordinary artisan possesses knowledge and skills rendering him capable of combining the prior art references. The current situation not only has specific motivation as noted, but there is clearly implicit motivation as discussed by Dystar.

(10) Response to Argument

Introduction

The BPAI remanded the appeal No. 93-4018 on August 08, 1996, indicating the issues on the status of priority applications of the instant application. After reviewing the issues raised by the Board, the examiner reopened the prosecution and indicated that the instant application fail to be given earlier priority or effective filling date than the filing date of the instant application of 9/1/89 and reevaluated the prior art and applied new rejections based on Wang et al. (US 5,219,727) under 135(b) or Mullis et al. (US 4,683,195) and later on 1/14/02, Subsequently, Examiner declared potential interference (No. 105,055) and the BPAI has issued a memorandum and a preliminary motion 1 on 4/5/2004. Applicants amended the claims which are not supported by the priority applications 07/143,045 filed on 1/12/1988 and 07/148,959 (hereafter '959) filed on 1/27/1988. Considering the BPAI decision on Interference No. 10,055 and the amended claims Examiner applied Wang et al. patent as a proper prior art and rejected the pending claims.

Response to the priority issue:

With regard to the Appellants assertions on page 13-14, 27-30 of the appeal brief, the arguments were found unpersuasive. First, the instant claims recite 'can be amplified by the same primers or by the different primers', which satisfy the requirements of the Wang et al. reference

and forms basis for the rejection, since the amendment uses alternative form of the language "or", the rejection is still applicable and Wang et al. reference stands as a prior art. Second, the instant claims recite 'can be amplified' which means that the same primers can be used or different primers can be used, which also refers to 'optional' language and supports the BPAI conclusion regarding the use of a shared primer pair. Thus the claims as presented encompass the same subject matter as in Wang et al. reference. Second, with regard to the priority to the 'same oligonucleotides, it is noted that same oligonucleotides do not represent same primers as recited in the instant claims and the fourth primer or maxigene primer do not represent a reference RNA since the term oligonucleotides represent both primers and probes and maxigene insert represents reference RNA. The '959 application discloses the fourth primer is provided as an additional aid to quantitation of virus levels in pateint samples and the reference RNA could be amplified and detected by the same the oligonucleotides used for the authentic virus RNA samples, however the example III of the '959 application discloses that the experiment I is repeated with the addition of a primer for maxigene, which clearly indicate that the experiment III utilizes maxigene primer in addtion to the primer pair that amplify the authentic virus RNA as in Example I and does not disclose the use of the same primers to amplify both the target and the reference RNA (HIVA, HIVB, T-cell receptor A and B and maxigene target as a reference RNA) simultaneously. The term 'same oligonucleotides' is not defined in the '959 application and the 'oligonucleotides' as such read on any primers or probes in general. The same oligonucleoitdes in '959 application do not represent same primers, since the Example III of the '959 application disclose repeating the Example I with the addition of maxigene primer or fourth primer as an additional aid to amplify and quantitate the target RNA. Further, the fourth primer or maxigene

primer is a primer and it is not a reference RNA as asserted by the Appellants. Accordingly the '959 does not support use of the same primers to amplify both virus target and reference RNA (maxigene) simultaneously. Further the Example III do not disclosed replacing the primers that amplify the reference RNA with that of the fourth primer, instead the Example III discoses that a maxigene primer is added and the Example I is repeated, indicating that the reaction mixture does comprise all the reagent components of Example I in addition to the fourth primer or maxigene primer.

With regard to the Appellants' assertions on page 19-21 of the appeal brief, Examiner refers to the method step of calculating the amount of target nucleic acid initially present in the sample after amplification represents the amount of target nucleic acid present in the sample before the amplifcation step and it does not mean that the target nucleic acid amount is measured before the amplifcation step. Appellants' arguments regarding Wang et al. were found unpersuasive because claim 1 step (f) of Wang et al. disclose calculating the amplified target nucleic acid and the standard segments produced in the preceding step (d) to detect the amount of the target nucleic acid before amplification. With regard to the Appellants' arguments drawn to Wang et al. reference does not qualify as a prior art, Appellants' arguments were found unpersuaisve because as discussed above, since the use of same primers lack support in the priority application, the Wang et al. reference is considered as the prior art since Wang et al. does teach use of same primers to amplify the target and the reference RNA as required by the instant claims, which recite use of same primers. With regard to the arguments drawn to the 131 declaration submitted on 12/15, 2005, Examiner notes that the declaration does not establish the conception and reduction to practice of the instant invention prior to January 1988. Further as

discussed in the previous office action mailed on 6/6/2007, Examiner indicated that the BPAI provided express difference between the claims in Wang et al. and Mukarawa et al. claims and Wang et al. requires use of the same primers that can amplify both the reference and the target nucleic acid and hence Wang et al. reference is not barred and is applied as prior art since the instant claims do require use of same primers as taught by Wang et al.

With regard to the Appellants' arguments on the page 23-27, 30-32, Appellants' arguments were fully considered and found unpersuaisve, as disccused above Wang et al. is a proper prior art and the declaration does not establish the conception and reduction to practice of the instant invention prior to January 1988, and as discussed above Wang et al. does teach use of same primers for amplifying target and the reference RNA and as discussed in the rejection, it would have been obvious to combine the method of Wang et al.with the teachings of Mullis et al.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Suryaprabha Chunduru/
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Conferees:

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